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HDL-C and Mortality

Salonen, Jukka

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Loes P. Hoebers, MD, PhD

*Jose P.S. Henriques, MD, PhD

on behalf of the EXPLORE Investigators

*Department of Cardiology

Academic Medical Center

Meibergdreef 9

1105 AZ Amsterdam

the Netherlands

E-mail: j.p.henriques@amc.uva.nl

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HDL-C and Mortality



Ko et al. conclude (1) that “high-density lipoprotein cholesterol (HDL-C) level is unlikely to represent a cardiovascular risk factor or a target for intervention.” As this has profound implications, I’d like to discuss possible explanations behind their findings. Alcohol intake increases total HDL-C, and therefore HDL-C is in part a measure of alcohol intake. High non-cardiovascular disease mortality at very high HDL-C levels may well be due to alcohol-induced non-cardiovascular disease mortality. I showed in a prospective population study (the KIID [Kuopio Ischemic Heart Disease] study) in Finland that low HDL-C is associated with increased coronary, cardiovascular, and all-cause mortality only if alcohol intake, as measured by serum gamma-glutamyl transferase levels, is low (2). I suggested in my discussion that HDL elevation might be beneficial only if gamma-glutamyl transferase is low and promoted liver enzyme measurements in studies of HDL-C and mortality. Therefore, I question the validity of the authors’ conclusions, which were based on a study with no data on either alcohol intake or liver damage.

*Jukka T. Salonen, MD, PhD, MSc

*Department of Public Health
Clinicum

Faculty of Medicine

University of Helsinki

Omenamäenkatu 23

00990 Helsinki

Finland

E-mail: jtsalonen@windowslive.com OR jukka.salonen@metabolic.fi

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REPLY: HDL-C and Mortality



We appreciate the comments raised by Dr. Salonen regarding the potential role of alcohol on our results. Dr. Salonen suggests that the relationship between high-density lipoprotein (HDL) cholesterol and outcomes may be discordant based on alcohol intake or liver enzyme levels (1).

In our study, we evaluated more than 630,000 individuals without prior cardiovascular conditions (2). We were able to impute alcohol use in the cohort using data from the Canadian Community Health Survey (CCHS), an ongoing Canada-wide population-based survey that collected information on self-reported health behavior. We found that 12.5% of individuals had heavy alcohol consumption (defined as ≥ 5 drinks on 12 occasions per year).

The evaluation of the independent association of HDL-cholesterol (HDL-C) level and cause-specific mortality was conducted by adjusting for liver disease (identified using administrative database codes), heavy alcohol consumption (imputed from the CCHS), demographics, and comorbidities. We found that individuals with lower HDL-C levels had increased hazard of cardiovascular deaths, cancer deaths, and noncardiovascular noncancer deaths. In addition, we also observed individuals who had very high HDL-C levels had increased hazard of noncardiovascular deaths. We agree that future research into reasons underlying higher noncardiovascular deaths among individuals with very high HDL-C levels is warranted and that alcohol intake could be an important contributor. In light of the inability of randomized trials to improve clinical outcomes by increasing HDL-C levels (3), and a Mendelian study showing no reduced clinical risk with genetic mechanism that raise HDL-C levels (4), our study adds to the existing